In the Claims

Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1. (Original) A method for reducing a side effect associated with thrombolytic therapy, comprising

inhibiting binding of tissue plasminogen activator (tPA) administered to a subject to a low-density lipoprotein-receptor-related protein (LRP) receptor.

2. (Original) The method of claim 1, wherein inhibiting binding of tPA to LRP comprises administering to a subject in need of such treatment an amount of an agent that reduces tissue plasminogen activator (tPA) binding to a low-density lipoprotein-receptor-related protein (LRP) receptor effective to reduce the side effect, wherein the agent is administered before, simultaneously with, or after tPA treatment.

3. (Original) The method of claim 1, wherein the side effect associated with thrombolytic therapy is cerebral hemorrhage and/or edema.

4. (Original) The method of claim 1, wherein the subject is human.

5. (Original) The method of claim 1, wherein the thrombolytic therapy is the administration of tPA.

6. (Original) The method of claim 2, wherein the agent that reduces tPA binding to a LRP receptor is administered before tPA treatment.

7. (Original) The method of claim 2, wherein the agent that reduces tPA binding to a LRP receptor is administered simultaneously with tPA treatment.

8. (Original) The method of claim 2, wherein the agent that reduces tPA binding to a LRP receptor is administered after tPA treatment.

9. (Original) The method of claim 2, wherein the administration is intravenous administration.

10. (Original) The method of claim 2, wherein the agent is an antibody or antigen-binding fragment thereof.

11. (Original) The method of claim 1, wherein the subject is suspected or known to be at risk for a condition selected from the group consisting of ischemia, hemorrhage, edema, and brain injury.

12. (Original) The method of claim 1, wherein the subject is suspected or known to have a condition selected from the group consisting of: ischemia, hemorrhage, edema, and brain injury.

13. (Original) The method of claim 1, wherein the subject is suspected or known to have had a condition selected from the group consisting of: ischemia, hemorrhage, edema, and brain injury.

14-28. (Cancelled)

29. (Original) A method of identifying a candidate agent that modulates tissue plasminogen activator (tPA) binding to a low-density lipoprotein-receptor-related protein (LRP) receptor comprising:

contacting an LRP receptor with tPA in the presence of a candidate agent,

determining the level of binding of the LRP receptor with the tPA, and

comparing the level of binding of LRP with tPA with a control level of binding of LRP and tPA not contacted with the candidate agent as a measure of the ability of the candidate agent to modulate tPA binding to LRP receptor.

30. (Original) The method of claim 29, wherein modulate is to reduce.

31. (Original) The method of claim 29, wherein modulate is to increase.

32. (Original) The method of claim 29, wherein the tPA is labeled with a detectable label.

33. (Original) The method of claim 29, wherein the LRP receptor is labeled with a detectable label.

34-41. (Cancelled)

42. (Original) A method of identifying a thrombolytic tissue plasminogen activator (tPA) variant with reduced binding to a low-density lipoprotein-receptor-related protein (LRP) receptor, comprising:

modifying a tPA molecule to prepare modified tPA molecules,

testing the thrombolytic activity of the modified tPA molecules,

selecting modified tPA molecules that retain thrombolytic activity (modified thrombolytic tPA molecules),

contacting an LRP receptor with the modified thrombolytic tPA molecules,

determining the level of binding of the LRP receptor with modified thrombolytic tPA molecules, and

comparing the level of binding of LRP receptor by modified thrombolytic tPA molecules with a control level of binding of LRP receptor by unmodified tPA as an indication of reduced binding of the modified thrombolytic tPA molecules to LRP receptor.

43. (Original) The method of claim 42, wherein the modification of the tPA molecule comprises one or more modifications selected from the group consisting of amino acid substitutions, amino acid deletions, and post-translational modifications.

44-45. (Cancelled)